drugs together to a maximal dose of half that used with the single drugs.

The major indication for a trial of combined monoamine-oxidase inhibitors and tricyclic treatment is depression that has proved refractory to adequate trials of treatment with more usual approaches—such as tricyclic antidepressants alone, monoamine-oxidase inhibitor alone, electroconvulsive therapy and so forth. A clinician choosing to try combination treatment should bear in mind that whereas some uncontrolled clinical experience has suggested its effectiveness for refractory depression, none of the four controlled studies so far reported has supported any advantage for combined monoamine-oxidase inhibitor and tricyclic treatment over administration of single drugs or electroconvulsive therapy. Nevertheless, official sanctions against the use of this approach are lifting in the face of evidence for reasonable safety with proper use. Pharmaceutic companies are revising package inserts accordingly, and last year the American College of Neuropsychopharmacology adopted as its official position paper the review by White and Simpson (1981).

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Use of Lithium Carbonate in Psychiatric Treatment

LITHIUM CARBONATE is used to treat recurrent mood disorders. It is most effective in controlling acute mania and for prophylaxis or bipolar I (mania) and bipolar II (hypomania) manic-depressive disorders, schizoaffective disorders and recurrent unipolar depression. It is less effective as a treatment for acute depression. When lithium is used to treat acute mania, relatively high serum concentrations (up to 1.8 mEq per liter) are acceptable as long as toxic symptoms are not produced. Neuroleptic medication is commonly added for the acute manic period. The use of lithium as prophylactic treatment has to be adjusted for each patient but is generally indicated for those who have two or more affective episodes within two years, those who have a history of more than three affective episodes and patients whose previous depressions had not responded quickly to antidepressants.

Prophylactic administration of lithium is not indicated after a single manic episode, but extreme care must be used to document the lack of previous manic or hypomanic episodes. It is not uncommon to have continued mood swings during the initial prophylactic treatment with lithium because its maximum prophylactic value may not occur for more than a year after onset of treatment. In most persons control can be achieved with maintenance lithium blood concentrations of 0.6 to 0.8 mEq per liter. Some persons, however, especially the elderly or organically impaired, cannot tolerate such levels, and in these cases concentrations as low as 0.3 mEq per liter may be effective. At the other extreme are some patients in whom maintenance levels as high as 1.6 mEq per liter are required.

Lithium treatment may be started in the following ways: using a large loading dose with careful subsequent monitoring of the blood concentration, giving a single 600-mg test dose with determination of a 24-hour blood concentration or starting the patient on a regimen of 600 mg a day and increasing the dose weekly after checking the blood lithium concentration. Standard lithium serum values are measured 10 to 14 hours after the last dose of lithium. The measurement of erythrocyte lithium value, as opposed to plasma or serum levels, is not commonly used in most clinical settings. Once persons have been stabilized on a particular blood concentration at a particular dose, there is little fluctuation and for uncomplicated maintenance therapy lithium levels should be checked only every four to six months.

There is no agreement among experts on laboratory tests that should be done before starting lithium treatment. Our consensus is that a pretreatment examination should include blood tests for serum creatinine and thyroid function and analysis of urine. There are no specific medical contraindications to lithium treatment (including cardiovascular disease), though in patients with cardiac disorders baseline and lithium treatment electrocardiograms should be done. Lithium has some antithyroid effects and causes hypothyroidism in a small percentage of patients. Thus, yearly thyroid function tests should be carried out, the best being the thyroid-stimulating hormone level. Hypothyroid changes are treated by administration of thyroid replacement. While lithium decreases the kidney's ability to concentrate urine, this is rarely of importance. In the absence of preexisting renal disease or evidence of renal disease while on lithium, the serum creatinine level should be checked yearly. Previous concerns about possible renal damage due to lithium are now thought to be exaggerated. Further, worries by some patients that lithium may affect "creativity" have not been substantiated.

Most persons receiving lithium have some side effects, which are usually mild and include thirst, increased urination and mild, fine, resting tremor. Subjective side effects such as nausea or gastrointestinal distress can often be relieved by using the slow-release form of lithium because peak blood concentrations after ingestion of medication are much lower with this form. Side effects of tremor are commonly treated with administration of propranolol, polyuria with hydrochlorothiazide and acne with topical antibiotics. Approximately 20 percent of patients receiving lithium have a significant weight gain of unknown cause, but it is, of course, calorie-dependent. Lithium is compatible with all other psychotropic medications, though some and possibly all neuroleptic agents raise the intraneuronal lithium level and thus may be responsible for mild toxic changes

at previously tolerated blood concentrations. Lithium can be given in combination with diuretics if blood concentrations are measured frequently during initiation and adjustment of diuretics. Lithium may increase the potential for digitalis toxicity by lowering intracellular potassium levels; thus, careful monitoring of electrocardiograms should be carried out during stabilization periods. Lithium use is contraindicated during pregnancy and for women who are breast-feeding.

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Sleep Disorders Medicine: A New Subspecialty

SLEEP DISORDERS MEDICINE has recently emerged as a new subspecialty. Nearly 100 sleep disorder centers have already been established in hospitals throughout the United States. Certified sleep disorder specialists (clinical polysomnographers) drawn from pulmonary medicine, neurology, cardiology, psychiatry, psychology and other fields offer comprehensive medical and psychiatric evaluation and treatment for a wide variety of clinical problems. A few disorders are as follows.

Excessive Daytime Sleepiness

Patients with excessive daytime sleepiness (EDS) show a persistent propensity to fall asleep at times when they wish to remain awake. Two major diagnoses should be considered: narcolepsy and obstructive sleep apnea. Narcolepsy is associated with cataplexy, consisting of brief episodes of objective muscle weakness usually precipitated by emotional arousal. It is found equally in men and women and usually begins during the late teenage years and early 20s. In contrast, patients with obstructive sleep apnea have hundreds of episodes during the night when effective respiration ceases because of upper airway obstruction. It is usually associated with profound snoring and occurs most frequently in obese middle-aged men. The symptoms of excessive daytime sleepiness may be related to the metabolic and blood gas abnormalities associated with prolonged, repeated apnea. Patients with both forms of this disorder fall asleep quickly in the sleep laboratory during daytime and nocturnal recordings.

Narcoleptic patients usually enter rapid-eye-movement (REM) sleep immediately on falling asleep. Patients who have sleep apnea show numerous episodes of apnea and may have severe, life-threatening periods of hypoxemia, hypercapnea, pulmonary and systemic hypertension and cardiac arrhythmias during apneic episodes. Once the diagnosis is established, relatively successful therapies are available for both forms of sleep disorder.

Major Depressive Disorders

Most depressed patients have insomnia, though a few have hypersomnia. More recently it has been found that many depressed patients show rather specific abnormalities of sleep, including a loss of stage 4 sleep (an electroencephalographic category) and a shortened REM latency (the elapsed time from sleep onset to the first REM period). These findings have stimulated considerable research into biologic factors in affective illness. The clinical usefulness of sleep laboratory investigations of depressed patients is currently being studied in such areas as differential diagnosis, assessment of severity and prediction of response to treatment.

Impotence

The differentiation of psychogenic and organic factors is an important consideration in the management of impotent patients. Because every normal man has full erections in association with REM periods, all-night-sleep laboratory recordings of sleep and nocturnal penile tumescence provide valuable information to clinicians who must decide whether to treat a patient psychiatrically, medically or surgically. During REM periods, it is possible to measure changes in penile circumference that occur with erections and, on awakening, to measure rigidity. Patients with organic impotency show little or no evidence of an objective erection during several nights in a sleep laboratory and are candidates for a penile prosthesis or a vascular operation.

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Neuroleptic Malignant Syndrome

THE NEUROLEPTIC MALIGNANT SYNDROME appears in patients being treated with antipsychotic medication and is characterized by fever, muscular rigidity, altered consciousness and autonomic dysfunction. Although the syndrome is considered rare, it is recently being reported with more frequency in the United States. Usually seen in men younger than 40 years, it has been reported in patients with various psychiatric diagnoses. Neuroleptic malignant syndrome has also been reported to occur with the administration of most major families of neuroleptic drugs, most often in therapeutic doses. It is seen less frequently with other psychotropic agents that are given either alone or in combination.

The syndrome usually resolves spontaneously when the offending neuroleptic agent is discontinued and does not always reappear when the causative agent is readministered. It is also not related to the duration of drug administration. Laboratory evaluation shows nonspecifi-